

Compositions comprising lactoferrin

The present invention relates to compositions comprising EGCG, to processes for their preparation and to their use for preventing or treating plaque, gingivitis, periodontal disease and oral malodor (halitosis) in pets, and for enhancing the antioxidative capacity in the whole organism.

- 5 More particularly the present invention provides in a first aspect a composition, e.g. a pet food, comprising epigallocatechin gallate (EGCG) and lactoferrin.

In another aspect the present invention provides a composition, e.g. a pet food, comprising epigallocatechin gallate (EGCG), lactoferrin, vitamin C, vitamin E and a carotenoid.

- 10 In still another aspect the present invention provides a composition, e.g. a pet food, comprising epigallocatechin gallate (EGCG), vitamin C, vitamin E and a carotenoid.

- In yet another aspect, the present invention relates to the use of a combination of EGCG and lactoferrin; or a combination of EGCG, lactoferrin, vitamin C, vitamin E and a carotenoid; or a combination of EGCG, vitamin C, vitamin E and a carotenoid in the  
15 manufacture of a pet food, particularly for dogs or cats, for preventing or treating plaque, gingivitis, periodontal disease and oral malodor (halitosis) in pets, and for enhancing the antioxidative capacity in the whole organism; and for the use of the aforesaid combinations for preventing or treating plaque, gingivitis, periodontal disease and oral  
20 malodor (halitosis) in pets, and for enhancing the antioxidative capacity in the whole organism.

Examples of pets include dogs, cats and rodents, e.g., chinchillas, guinea pigs, degus, mice, gerbils, hamsters, rats, ferrets and lagomorphes, e.g., rabbits. Animals of all ages are included, e.g. adults, animals of medium age and seniors.

- EGCG is a polyphenol derived from the green tea plant *Camellia sinensis*. It may be added  
25 to the pet food in any form, including, e.g., green tea extracts containing varying amounts of EGCG as well as highly enriched EGCG preparations such as the EGCG preparation

obtained by the process as described in EP 1,077,211. In this process EGCG is highly enriched starting from any green tea extract, e.g. green tea leaves are typically extracted with hot or cold water to form a solution containing tea catechins and caffeine. This green tea solution can be further concentrated to form either a concentrated extract solution or a dry powder. Tea extract powders are commercially available e. g. from Guizhou Highyin Biological Product Co., Guiyang, P. R. China, or Zhejiang Zhongke Plant Technical Co. Ltd., Hangzhou, Zhejiang, P. R. China. Suitably, EGCG is present in the compositions of the present invention in a concentration of from about 0.001 to about 3 % (w/w).

Lactoferrin is an 80 kDa glycoprotein consisting of a single peptide chain with two globular lobes. For the purpose of the present invention the term lactoferrin is to also comprise lactoferricin which is a product of peptic hydrolysis of lactoferrin. Lactoferrin formulations are commercially available, e.g., from Tatua Nutritionals (Tatua Co-operative Dairy Company Limited, State Highway 26 Tatuanui Private Bag 800, Morrisville, New Zealand), or may be prepared or isolated from milk following proceedings known to the skilled person. Suitably, lactoferrin is present in the compositions of the present invention in a concentration of from about 0.002 to 3 % (w/w).

The term "vitamin C" is used herein for a group of compounds including L-ascorbic acid, L-ascorbyl palmitate, calcium ascorbate dihydrate, L-ascorbic acid monosodium salt and L-ascorbic acid phosphate esters like L-ascorbic acid monophosphate, L-ascorbic acid diphosphate and L-ascorbic acid triphosphate, and is commercially available, e.g. from Roche Vitamins AG, Switzerland, under the tradename STAY-C®. Suitably, vitamin C is present in the compositions of the present invention in a concentration of from about 30 to about 6000 mg/kg, vitamin E in a concentration of from about 20 to about 450 IU/kg and a carotenoid in a concentration of from about 2 to about 315 mg/kg, based on the total weight of the composition.

The term "vitamin E" as used herein is a collective term for several biologically similar compounds called tocopherols and tocotrienols which share the same biological activity and include *dl*- $\alpha$ -tocopherol, *d*- $\alpha$ -tocopheryl acetate and *dl*- $\alpha$ -tocopheryl acetate. Vitamin E formulations are commercially available from Roche Vitamins AG under the tradenames ROVIMIX® E-50 Adsorbate or ROVIMIX® E 50 SD. Suitably, vitamin E is present in the compositions of the present invention of from about 20 to about 450 IU/kg.

The term "carotenoid" as used herein comprises a carotene or structurally related polyene compound such as  $\alpha$ - or  $\beta$ -carotene, 8'-apo- $\beta$ -carotenal, 8'-apo- $\beta$ -carotenoic acid esters such as the ethyl ester, canthaxanthin, astaxanthin, lycopene, lutein, zeaxanthin or crocetin, or mixtures thereof. Preferred carotenoids for the purpose of this invention are  $\beta$ -carotene and lutein. Carotenoids are suitably present in the compositions of the present invention in a concentration of from about 2 to about 315 mg/kg, based on the total weight of the composition.

EGCG, lactoferrin, vitamin C, vitamin E and carotenoids contained in the compositions of the invention are herein referred to collectively as Inventive Ingredients.

- 10 The term "composition" as used herein comprises the mixture of the components (Inventive Ingredients) as well as feed and feedstuff including premixes used therefor, especially for pets, which contain the mixture of Inventive Ingredients.

The pet food according to the present invention may be based on any conventional pet food. There is a wide range of pet foods available which may be grouped into (a) complete diets, (b) complementary diets, and (c) snacks and treats. Complete diets may be fed in addition to water for an extended period as the sole source of nutrients and will provide for all the energetic and nutrient needs of the animal and the physiological state for which it is intended. Complementary diets normally are not sufficient to ensure that all nutrient and energy requirements are met unless fed in combination with another foodstuff or diet. Snacks and treats are appetizers or for occasional feeding and are considered as complementary products. There are, however, a number of products available intended to form part of the daily diet or playing a role in animal well-being, e.g. dental chews. In the present invention dental chews are especially suitable.

- The pet food of the present invention may be in a dry, canned, semi-moist or baked form. Typical components of such compositions, in addition to Inventive Ingredients, are crude protein, crude fat, carbohydrates (NfE), starch, crude fibers, and ash, further on minerals, trace elements, vitamins, fatty acids, protein and amino acids, choline, carnitin, dietary fiber and substances required for balanced diets of the different animal species. Basic ingredients of such food compositions are
- 25 -Crude Protein including proteins and N-containing compounds of non-proteinaceous nature, e.g. acid amides, amines, free amino acids, ammonium salts, alkaloids;
- 30

- Crude Fat including neutral fats, lipoids (phospho-, sphingolipids; steroids) and other ethersoluble compounds;
- N-free Extractions (NFE) including polysaccharides (starch, glycogen), soluble saccharides (glucose, fructose, saccharose, lactose, maltose and oligosaccharides), and  
5 soluble fractions of cellulose, hemicellulose, lignin and pectines;
- Crude Fibers including insoluble fractions of cellulose, hemicellulose, lignin and other components of the cell wall like suberin, cutin etc.;
- Ash including minerals (macrominerals such as calcium, phosphorus, sodium, chloride, potassium, magnesium, and microminerals, i.e., trace elements, such as iron, copper  
10 manganese, zinc, iodine, selenium,) and further inorganic substances e.g. silicate.
- Vitamins including vitamins A, B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub>, B<sub>12</sub>, D, pantothenic acid, niacin, biotin, folic acid, linolic acid and choline.

Further components may, e.g. be omega-6-fatty acids, omega-3-fatty acids, L-carnitine, chondroitin sulfate, glucosamine, glutamine/glutamic acid, arginine, taurine and  
15 hydroxyproline.

Typical components which provide the ingredients for a dog food composition, in addition to Inventive Ingredients, comprise, e.g., chicken/beef/turkey, liver, broken pearl barley, ground corn, brute fat, whole dried egg, fowl protein hydrolyzate, vegetable oil, calcium carbonate, choline chloride, potassium chloride, iodinated salt, iron oxide, zinc  
20 oxide, copper sulfate, manganese oxide, sodium selenite, calcium iodate, provitamin D, vitamin B<sub>1</sub>, niacin, calcium panthothenate, pyridoxin hydrochloride, riboflavin, folic acid, biotin, vitamin B<sub>12</sub>.

Typical components which provide the ingredients for a cat food composition, in addition to Inventive Ingredients, comprise beef, chicken meat, dried chicken liver, lamb meat,  
25 lamb liver, pork, turkey meat, turkey liver, poultry meal, fish meal, fowl protein hydrolysate, animal fats, plant oils, soy bean meal, pea bran, maize gluten, whole dry egg, ground corn, corn flour, rice, rice flour, dry sugar beet molasses, fructooligosaccharides, soluble fibres, plant gums, cellulose powder, clay, bakers yeast, iodized sodium chloride, calcium sulfate, sodium triphosphate, dicalcium phosphate, calcium carbonate, potassium  
30 chloride, choline chloride, magnesium oxide, zinc oxide, iron oxide, copper sulfate, iron sulfate, manganese oxide, calcium jodate, sodium selenite, provitamin D, thiamine, niacin, calcium pantothenate, pyridoxine hydrochloride, riboflavin, folic acid, biotin, vitamin B<sub>12</sub>, taurin, L-carnitine, caseine, D-methionine.

Wet pet food contains between about 70 and about 85 % moisture and about 15 and about 25 % dry matter.

A typical wet food for adult dogs may, e.g. comprise, in addition to Inventive Ingredients, at minimum 24 % protein, 15 % fat, 52 % starch, 0.8 % fibre, 3 % linolic acid, 0.6 % calcium, 0.5 % phosphorus, the Ca:P ratio being 1:1, 0.2 % potassium, 0.6 % sodium, 0.09 % chloride, 0.09 % magnesium, 170 mg/kg of iron, 15 mg/kg of copper, 70 mg/kg of manganese, 220 mg/kg of zinc, 4 mg/kg of iodine, 0.43 mg/kg of selenium, 74000 IU/kg of vitamin A, 1200 IU/kg of vitamin D, 11 mg/kg of vitamin B<sub>1</sub>, 6 mg/kg of riboflavin, 30 mg/kg of pantothenic acid, 20 mg/kg of niacin, 4.3 mg/kg of pyridoxine, 0.9 mg/kg of folic acid, 0.2 µg/kg of vitamin B<sub>12</sub>, 2500 mg/kg of choline, 0.8 mg/kg biotin, 2500 mg/kg cholin, all percentages being based on dry weight of the total food composition.

A typical wet food for adult cats may, e.g. comprise, in addition to Inventive Ingredients, at minimum 44 % protein, 25 % fat, 20 % starch, 2.5 % fibre, 0.8 % calcium, 0.6 % phosphorus, 0.8 % potassium, 0.3 % sodium, 0.09 % chloride, 0.08 % magnesium, 0.25 % taurin, 170 mg/kg of iron, 15 mg/kg of copper, 70 mg/kg of manganese, 220 mg/kg of zinc, 4 mg/kg of iodine, 0.43 mg/kg of selenium, 74000 IU/kg of vitamin A, 1200 IU/kg of vitamin D, 11 mg/kg of vitamin B<sub>1</sub>, 6 mg/kg of riboflavin, 30 mg/kg of pantothenic acid, 20 mg/kg of niacin, 4.3 mg/kg of pyridoxine, 0.9 mg/kg of folic acid, 0.2 µg/kg of vitamin B<sub>12</sub>, 2500 mg/kg of choline, 0.8 mg/kg biotin, 2500 mg/kg cholin, all percentages being based on dry weight of the total food composition.

Dry pet food contains between about 6 and about 14 % moisture and about 86 % or more dry matter.

A typical dry food for adult dogs may, e.g. comprise, in addition to Inventive Ingredients, at minimum 25 % protein, 12 % fat, 41.5 % starch, 2.5 % fibre, 1 % linolic acid, 1 % calcium, 0.8 % phosphorus, the Ca:P ratio being 1:1, 0.6 % potassium, 0.35 % sodium, 0.09 % chloride, 0.1 % magnesium, 170 mg/kg of iron, 35 mg/kg of copper, 70 mg/kg of manganese, 220 mg/kg of zinc, 4 mg/kg of iodine, 0.43 mg/kg of selenium, 15000 IU/kg of vitamin A, 1200 IU/kg of vitamin D, 11 mg/kg of vitamin B<sub>1</sub>, 6 mg/kg of riboflavin, 30 mg/kg of pantothenic acid, 20 mg/kg of niacin, 4.3 mg/kg of pyridoxine, 0.9 mg/kg of folic acid, 0.2 µg/kg of vitamin B<sub>12</sub>, 2500 mg/kg of choline, 0.8 mg/kg biotin, all percentages being based on dry weight of the total food composition.

A typical food for adult cats may, e.g. comprise, in addition to Inventive Ingredients, at minimum 32 % protein, 15 % fat, 27.5 % starch, 11 % dietetic fibres, 4.5 % fibre, 3.4 % linolic acid, 0.08 % arachionic acid, 0.15 % taurin, 50 mg/kg L-carnitin, omega 6/3 = 5, 1 % calcium, 0.8 % phosphorus, the Ca:P ratio being at least 1:1, 0.6 % potassium, 0.4 % sodium, 0.6 % chloride, 0.08 % magnesium, 190 mg/kg of iron, 30 mg/kg of copper, 60 mg/kg of manganese, 205 mg/kg of zinc, 2.5 mg/kg of iodine, 0.2 mg/kg of selenium, 25000 IU/kg of vitamin A, 1500 IU/kg of vitamin D, 20 mg/kg of vitamin B<sub>1</sub>, 40 mg/kg of riboflavin, 56 mg/kg of pantothenic acid, 153 mg/kg of niacin, 14 mg/kg of pyridoxine, 3.2 mg/kg of folic acid, 0.2 mg/kg of vitamin B<sub>12</sub>, 1 mg/kg of biotin, 3000 mg/kg of choline, all percentages being based on dry weight of the total food composition.

A typical dry food for adult dogs with teeth problems comprises, in addition to Inventive Ingredients, chicken by-product meal, corn meal, brewers rice, powdered cellulose, soybean mill run, animal fat (preserved with BHA, propyl gallate and citric acid), dried egg product, vegetable oil, natural flavor, flaxseed, taurine, preserved with BHT and BHA, beta-carotene, minerals (potassium chloride, salt, ferrous sulfate, zinc oxide, copper sulfate, manganous oxide, calcium iodate, sodium selenite), vitamins (choline chloride, vitamin A supplement, vitamin D<sub>3</sub> supplement, vitamin E supplement, niacin, thiamine, calcium pantothenate, pyridoxine hydrochloride, riboflavin, folic acid, biotin, vitamin B<sub>12</sub> supplement).

A typical dry food for adult cats with teeth problems comprises, in addition to Inventive Ingredients, chicken by-product meal, brewers rice, corn gluten meal, animal fat (preserved with BHA, propyl gallate and citric acid), corn meal, powdered cellulose, chicken liver flavor, vegetable oil, DL-methionine, taurine, preserved with BHT and BHA, β-carotene, minerals (potassium chloride, calcium carbonate, salt, calcium sulfate, ferrous sulfate, zinc oxide, copper sulfate, manganous oxide, calcium iodate, sodium selenite), vitamins (choline chloride, vitamin A supplement, vitamin D<sub>3</sub> supplement, niacin, thiamine, calcium pantothenate, riboflavin, pyridoxine hydrochloride, folic acid, biotin, vitamin B<sub>12</sub> supplement).

Typical components which provide the ingredients for a dog treat composition, e.g. cake or biscuit, may comprise vegetable by-products (wheat meal), meat and animal by-products (meat meal), grain (wheat), minerals, oils and fat (plant and animal fats).

A typical dog treat may, e.g. comprise at minimum 10 % water, 24 % protein, 6 % fat, 27.5 % starch, 6.5 % ash, 2.5 % fibre, 1.2 % calcium, 0.8 % phosphorus and 0.25 % sodium.

Typical components which provide the ingredients for a cat treat composition, e.g. cake or biscuit, may comprise vegetable products, meat and animal by-products, grain (wheat),  
5 minerals and vegetable by-products.

A typical cat treat may, e.g. comprise, in addition to Inventive Ingredients, at minimum 12 % water, 10 % protein, 2.5 % fat, 6 % ash, 2 % fibre.

A preferred pet food composition of the present invention is in the form of a treat.

Inventive ingredients may be incorporated into conventional pet food e.g., into dry pet  
10 food by spraying an aqueous solution containing one or more Inventive Ingredients on the food composition while thoroughly mixing the composition, or by adding one or more Inventive Ingredients to the dough. Inventive ingredients may be added simultaneously, e.g. at the same time and even as a premix, or consecutively as single inventive ingredient at a time or as a premix. Premixes may also include one or more of the other components  
15 of the final composition.

Dry food may be prepared, e.g., by screw extrusion including cooking, shaping and cutting of raw ingredients into a specific kibble shape and size in a very short period of time, while simultaneously destroying detrimental micro-organisms. The ingredients may be mixed into homogenous expandable dough and cooked in an extruder (steam/pressure) and  
20 forced through a plate under pressure and high heat. After cooking, the kibbles are then allowed to cool, before optionally being sprayed with a coating which may include liquid fat or digest including liquid or powdered hydrolyzed forms of an animal tissue such as liver or intestine from, e.g., chicken or rabbit. Hot air drying then reduces the total moisture content to 10 % or less.

25 Canned (wet) food may be prepared, e.g., by blending the raw ingredients including meats and vegetables, fatty acids, gelling agents, gravies, vitamins, minerals and water. The mix is then fed into cans on a production line, the lids are sealed on and the filled cans are sterilized at a temperature of about 130°C for about 50 to 100 min.

The pet foods of the present invention are useful in preventing or treating plaque,  
30 gingivitis, periodontal disease and oral malodor (halitosis) in pets, and for enhancing the antioxidative capacity in the whole organism.

The present invention provides the use of the composition of the invention in preventing or treating plaque, gingivitis, periodontal disease and oral malodor (halitosis) in pets, and for enhancing the antioxidative capacity in the whole organism.

5 Plaque is a soft, gelatinous material composed of bacteria and their metabolic byproducts, oral debris, and salivary components. Mature plaque is not removed by normal actions of the tongue or by rising of the mouth. Rather, mechanical abrasion from chewing or tooth brushing is necessary for plaque removal.

10 Left undisturbed, aerobic and facultative anaerobic bacteria proliferate as the plaque thickens and matures. Over time, salivary calcium salts are deposited on the plaque, producing calculus. Calculus is a hard deposit that provides a rough surface, promoting accumulation of more plaque and also contributing to tissue damage as it extends into the gingival sulcus. Gingivitis occurs when plaque and calculus form at the neck of the tooth, leading to inflammation and tissue damage. As the gingival sulcus enlarges into a periodontal pocket, the area provides an oxygen-depleted environment that allows  
15 proliferation of anaerobic bacteria. Periodontal disease becomes established when the periodontal ligament is exposed to plaque, bacteria, and bacterial byproducts.

In some animals gingivitis persists without progressing into periodontitis. However, in most, untreated gingivitis eventually progresses to periodontal disease. Clinical signs of gingivitis and periodontal disease include oral malodor, gingival sensitivity and bleeding,  
20 tooth loss, and difficulty in eating.

Oral malodor (halitosis) is commonly reported in pets and is perceived by many owners to be a significant problem. Being associated with gingivitis and periodontitis one explanation for halitosis may be that chronic inflammation and tissue damage provides increased protein substrate for microorganisms in the mouth, enhancing the production  
25 of VSCs, volatile sulfur compounds. These compounds, particularly mercaptyl sulfide and hydrogen sulfide, produce breath malodor when exhaled.

The presence and proliferation of certain species of anaerobic bacteria and the inflammatory responses of the host contribute to the progressive destruction of the periodontium. As the supporting connective tissues and adjacent bone are weakened, teeth  
30 become loose and may be lost. Periodontal disease itself causes discomfort and pain and, if left untreated, can lead to bacteremia.



Odontoclastic resorptive lesions in cats also have been associated with gingival inflammation and, possibly, periodontal disease.

Since the majority of periodontal pathogens are gram-negative bacteria which release endotoxins (lipopolysaccharides – LPS) dental diseases are a potential risk factor for systemic disease in pets resulting in a systemic bacteremia or LPS challenge.

The importance of maintaining healthy periodontal tissues is of greater significance when considered that chronic periodontal disease may have a systemic as well as local effects. The most important factor that influences the development of gingivitis and periodontal disease in the dog and cat is the presence and persistence of undisturbed plaque on tooth surface. Once plaque has been deposited on the surface of the tooth, it may be reduced mechanically through abrasion provided by diet, chewing on supplemental chew toys or foods. The use of antimicrobial agents like chlorhexidine digluconate in conjunction with brushing, and the use of a chemical mouthwash is not effective in removing the hardened calculus that forms when plaque is allowed to accumulate.

Antioxidative capacity in the whole organism is a means to reflect the organism's capability to withstand oxidative stress and protect cell membrane and cytosolic components against free radical damage. The higher the antioxidative capacity the higher its ability to neutralize free radicals and arrest the chain effect of free radical damage thereby playing a vital role in maintaining the health and integrity of individual cells.

The amount of plaque forming bacteria may be determined by counting the bacteria commonly considered responsible for the pathogenesis of periodontitis, e.g. *Streptococcus mutans*, *Eikenella corrodens* and *Porphyromonas gingivalis*, and further *Prevotella ssp*, *Bacteroides gingivalis*, *Bacteroides intermedius*, *Actinobacillus* and *Actinobacillus*. For example, subgingival plaque may be taken from the maxillary premolars of dogs with a scaler. Saliva, tongue dorsum and bucal mucosa may be obtained as cotton swabs. Each specimen may be placed immediately, e.g., in sterile oxygen free tubes containing, e.g. 10 ml GAM broth and stored in an anaerobic glove box with 70 % N<sub>2</sub>, 15% CO<sub>2</sub>, and 15% H<sub>2</sub>. The diluted suspension of each sample may, e.g., be placed on Brain Heart Infusion agar with 7% horse blood for total counts, and Brucella HK agar with 7% horse blood for counts of genus *Porphyromonas* as black-pigmented bacteria. Identification and bacterial count of representative colonies may be carried out using Rapid ANA II system, AIP 20A and API-ZYM systems. For *Streptococcus mutans* a Brain Heart Infusion would be used,

too. The conditions used would be aerobic. After incubation at 37°C for 48 hours, MICs would be estimated using the systems mentioned above.

Gingivitis (oral inflammation) may be determined by measuring the gingival index, a method for estimating severity of inflammation of the gums.

5 To determine changes in, especially, white blood cells, a total blood count may be carried out.

- Red blood cell count: Hemoglobin, hematocrit, number of erythrocytes, erythrocyte indices MCHC, MCH, MCV.

10 - White blood cell count: Total number of leukocytes, differential blood count (Basophiles, neutrophiles, eosinophiles, monocytes, thrombocytes, B - and T-lymphocytes) relative and absolute.

The cellular profile may be used to determine changes in the humoral immune system. Therefore IgA and IgG concentration may be estimated.

15 Parameters for the determination of the antioxidant capacity include TEAC (Trolox equivalent antioxidant capacity) which may be measured, e.g. after a 1:1 dilution with a spectrophotometer, on which absorbance values were recorded over 3 minutes, according to the method of Armstrong and Browne, Adv Exp Med Biol 366:43-58 (1994), Total Antioxidant Capacity (TAC), Erythrocyte Superoxid Dismutase (SOD) which may, e.g., be determined based on the method developed by McCord and Fridovich, J Biol Chem  
20 244:6056-63 (1969) coupling O<sub>2</sub>-generators (xanthine and xanthine oxidase (XOD)) with an O<sub>2</sub>-detector [2-(4-iodophenyl)-3-(4-nitrophenol)-5-phenyltetrazolium chloride] and monitoring absorbance in a spectrophotometer; Ferritin which may be determined by an enzyme-linked immunoassay, Ceruloplasmin which may be determined by a colorimetric method to determine ceruloplasmin oxidase activity; Vitamin E and C; CK; GOT which  
25 may be determined by using a fluorescence detector at a wavelength of 334 nm.

The following examples illustrate the invention further.

#### Example 1

Commercial dry dog food (Hill's Science diet "Canine Maintenance dry" for dogs as supplied by Hill's Pet Nutrition GmbH, Liebigstrasse 2-20, D- 22113) is sprayed with an  
30 aqueous solution of lactoferrin (as supplied by Tatua Nutritionals) and EGCG (as supplied by Roche Vitamins) in an amount sufficient to provide 0.002 to 3.0 % by weight of

lactoferrin and 0.001 to 1.0 % by weight of EGCG in the final food composition. Further Vitamin C and E and  $\beta$ -carotene are incorporated in an amount sufficient to provide 30 mg vitamin C/kg, and 300 IU vitamin E/kg and 280 mg  $\beta$ -carotene/kg in the final food composition before extruding the entire blend. The food composition is dried to contain  
5 dry matter of about 90 % by weight.

#### Example 2

Commercial wet dog food (Hill's Science diet "Canine Maintenance wet" for dogs as supplied by Hill's Pet Nutrition GmbH, Liebigstrasse 2-20, 22113 Hamburg, Germany) is mixed with an aqueous solution of lactoferrin (as supplied by Tatua Nutritionals) and  
10 EGCG (as supplied by Roche Vitamins) in an amount sufficient to provide 0.002 to 3.0 % by weight of lactoferrin and 0.001 to 1.0 % by weight of EGCG in the final food composition. Further Vitamin C and E and  $\beta$ -carotene are incorporated in an amount sufficient to provide 30 mg vitamin C/kg, and 300 IU vitamin E/kg and 280 mg  $\beta$ -carotene/kg in the final food composition before cooking the entire blend. The food  
15 composition is dried to contain a dry matter of about 90 % by weight.

#### Example 3

Commercial dog treats (Mera Dog "Biscuit" for dogs as supplied by Mera Tiernahrung GmbH, Marienstrasse 80-84, 47625 Kevelaer-Wetten, Germany) are sprayed with an aqueous solution of lactoferrin (as supplied by Tatua Nutritionals) and EGCG (as supplied  
20 by Roche Vitamins) in an amount sufficient to provide 0.002 to 3.0 % by weight of lactoferrin and 0.001 to 1.0 % by weight of EGCG in the final food composition. Further Vitamin C and E and  $\beta$ -carotene are incorporated in an amount sufficient to provide 30 mg vitamin C/kg, and 300 IU vitamin E/kg and 280 mg  $\beta$ -carotene/kg in the final food composition before extruding the entire blend. The food composition is dried to contain a  
25 dry matter of about 90 % by weight.

#### Example 4

Commercial dry cat food (Hill's Science diet "Feline Maintenance dry" for cats as supplied by Hill's Pet Nutrition GmbH, Liebigstrasse 2-20, D- 22113) is sprayed with an aqueous solution of lactoferrin (as supplied by Tatua Nutritionals) and EGCG (as supplied by  
30 Roche Vitamins) in an amount sufficient to provide 0.002 to 3.0 % by weight of lactoferrin

and 0.001 to 1.0 % by weight of EGCG in the final food composition. Further Vitamin C and E and  $\beta$ -carotene are incorporated in an amount sufficient to provide 30 mg vitamin C/kg; and 300 IU vitamin E/kg and 280 mg  $\beta$ -carotene/kg in the final food composition before extruding the entire blend. The food composition is dried to contain a dry matter of about 90 % by weight.

#### Example 5

Commercial wet cat food (Hill's Science diet "Feline Maintenance wet" for cats as supplied by Hill's Pet Nutrition GmbH, Liebigstrasse 2-20, D- 22113) is sprayed with an aqueous solution of lactoferrin (as supplied by Tatura Nutritionals) and EGCG (as supplied by Roche Vitamins) in an amount sufficient to provide 0.002 to 3.0 % by weight of lactoferrin and 0.001 to 1.0 % by weight of EGCG in the final food composition. Further Vitamin C and E and  $\beta$ -carotene are incorporated in an amount sufficient to provide 30 mg vitamin C/kg, and 300 IU vitamin E/kg and 280 mg  $\beta$ -carotene/kg in the final food composition before cooking the entire blend. The food composition is dried to contain a dry matter of about 90 % by weight.

#### Example 6

Commercial cat treats (Whiskas Dentabits for cats as supplied by Whiskas, Masterfoods GmbH, Eitzer Str. 215, 27283 Verden/Aller, Germany) are sprayed with an aqueous solution of lactoferrin (as supplied by Tatura Nutritionals) and EGCG (as supplied by Roche Vitamins) in an amount sufficient to provide 0.002 to 3.0 % by weight of lactoferrin and 0.001 to 1.0 % by weight of EGCG in the final food composition. Further Vitamin C and E and  $\beta$ -carotene are incorporated in an amount sufficient to provide 30 mg vitamin C/kg, and 300 IU vitamin E/kg and 280 mg  $\beta$ -carotene/kg in the final food composition before extruding the entire blend. The food composition is dried to contain a dry matter of about 90 % by weight.

What is claimed is:

1. A composition comprising epigallocatechin gallate (EGCG) and lactoferrin.
2. A composition as in claim 1 comprising additionally vitamin C, vitamin E and a carotenoid.
- 5 3. A composition comprising epigallocatechin gallate (EGCG), vitamin E and a carotenoid.
4. A composition as in any one of claims 1-3 comprising epigallocatechin gallate (EGCG) in a concentration of from about 0.001 to about 3 % (w/w) and lactoferrin in a concentration of from about 0.002 to 3 % (w/w).
5. A composition as in any one of claims 1 to 5 comprising vitamin C in a concentration of  
10 from about 30 to about 6000 mg/kg, vitamin E in a concentration of from about 20 to about 450 IU/kg and a carotenoid in a concentration of from about 2 to about 315 mg/kg, based on the total weight of the composition.
6. A composition as in any of claims 1 to 5 which is a pet food, particularly for dogs or cats.
- 15 7. The use of a composition of any one of claims 1 to 3 in the manufacture of a pet food, particularly for dogs or cats, for preventing or treating plaque, gingivitis, periodontal disease and oral malodor (halitosis) in pets, and for enhancing the antioxidative capacity in the whole organism.
8. The use as in claim 7 of a combination of EGCG and lactoferrin.
- 20 9. The use as in claim 7 of a combination of EGCG, lactoferrin, vitamin C, vitamin E and a carotenoid.
10. The use as in claim 7 of a combination of EGCG, vitamin C, vitamin E and a carotenoid.
11. The use of a composition or a pet food of any one of claims 1 to 6 for preventing or  
25 treating plaque, gingivitis, periodontal disease and oral malodor (halitosis) in pets, particularly dogs or cats, and for enhancing the antioxidative capacity in the whole organism of the animal.

What is claimed is:

1. A composition comprising epigallocatechin gallate (EGCG) and lactoferrin.
2. A composition as in claim 1 comprising additionally vitamin C, vitamin E and a carotenoid.
- 5        3. A composition as in any one of claims 1 or 2 comprising epigallocatechin gallate (EGCG) in a concentration of from about 0.001 to about 3 % (w/w) and lactoferrin in a concentration of from about 0.002 to 3 % (w/w).
4. A composition as in any one of claims 1 or 2 comprising vitamin C in a concentration of from about 30 to about 6000 mg/kg, vitamin E in a concentration of from  
10        about 20 to about 450 IU/kg and a carotenoid in a concentration of from about 2 to about 315 mg/kg, based on the total weight of the composition.
5. A composition as in any of claims 1 to 4 which is a pet food, particularly for dogs or cats.
6. The use of a composition of any one of claims 1 to 5 in the manufacture of a pet  
15        food, particularly for dogs or cats, for preventing or treating plaque, gingivitis, periodontal disease and oral malodor (halitosis) in pets, and for enhancing the antioxidative capacity in the whole organism.
7. The use as in claim 6 of a combination of EGCG and lactoferrin.
8. The use as in claim 6 of a combination of EGCG, lactoferrin, vitamin C, vitamin E  
20        and a carotenoid.
9. The use of a combination of EGCG, vitamin C, vitamin E and a carotenoid in the manufacture of a pet food, particularly for dogs or cats, for preventing or treating plaque, gingivitis, periodontal disease and oral malodor (halitosis) in pets, and for enhancing the antioxidative capacity in the whole organism.
- 25        10. The use of a composition or a pet food of any one of claims 1 to 5 for preventing or treating plaque, gingivitis, periodontal disease and oral malodor (halitosis) in pets, particularly dogs or cats, and for enhancing the antioxidative capacity in the whole organism of the animal.
11. The use of a combination of EGCG, vitamin C, vitamin E and a carotenoid for  
30        preventing or treating plaque, gingivitis, periodontal disease and oral malodor (halitosis) in pets, particularly dogs or cats, and for enhancing the antioxidative capacity in the whole organism of the animal.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/E 3/07875

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A23K1/16 A23K1/18 A61K38/40

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A23K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, FSTA, BIOSIS, COMPENDEX

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 00183 A (SIGMA TAU HEALTHSCIENCE SPA ;CAVAZZA CLAUDIO (IT)) 6 January 2000 (2000-01-06) example 13	3,6
X	WO 01 85183 A (NUTRICIA NV ;VERDEGEM PETER JULIEN EDWARD (NL)) 15 November 2001 (2001-11-15) claims 1,8,9; examples	3,5,6
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

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- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \* & \* document member of the same patent family

Date of the actual completion of the international search

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/E 03/07875

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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International Application No

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